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PTO/SB/21 (04-07)  
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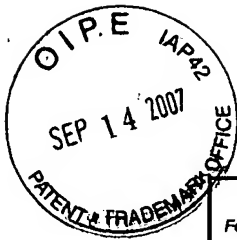
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<h2 style="margin: 0;">TRANSMITTAL FORM</h2> <p style="font-size: small; margin-top: 10px;">(to be used for all correspondence after initial filing)</p>	Application Number	10/692,724-Conf. #9697
	Filing Date	October 27, 2003
	First Named Inventor	Joseph LOSCALZO
	Art Unit	1657
	Examiner Name	K. C. Srivastava
Total Number of Pages in This Submission	Attorney Docket Number 0102258.00170US3	

ENCLOSURES (Check all that apply)		
<input checked="" type="checkbox"/> Fee Transmittal Form  <input type="checkbox"/> Fee Attached  <input type="checkbox"/> Amendment/Reply  <input type="checkbox"/> After Final  <input type="checkbox"/> Affidavits/declaration(s)  <input type="checkbox"/> Extension of Time Request  <input type="checkbox"/> Express Abandonment Request  <input checked="" type="checkbox"/> Information Disclosure Statement  <input type="checkbox"/> Certified Copy of Priority Document(s)  <input type="checkbox"/> Reply to Missing Parts/Incomplete Application  <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s)  <input type="checkbox"/> Licensing-related Papers  <input type="checkbox"/> Petition  <input type="checkbox"/> Petition to Convert to a Provisional Application  <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address  <input type="checkbox"/> Terminal Disclaimer  <input type="checkbox"/> Request for Refund  <input type="checkbox"/> CD, Number of CD(s) _____  <input type="checkbox"/> Landscape Table on CD	<input type="checkbox"/> After Allowance Communication to TC  <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences  <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)  <input type="checkbox"/> Proprietary Information  <input type="checkbox"/> Status Letter  <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): Return Receipt Postcard  41 References
<div style="border: 1px solid black; width: 150px; height: 20px; margin-bottom: 5px; float: left;">Remarks</div>		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT			
Firm Name	WILMER CUTLER PICKERING HALE AND DORR LLP		
Signature	<i>Belinda Lew</i>		
Printed name	Belinda Lew		
Date	September 14, 2007	Reg. No.	53,212

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Dated: September 14, 2007	Signature: <i>Belinda Lew</i> (Belinda Lew)



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<b>Effective on 12/08/2004.</b> <b>Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).</b> <b>FEE TRANSMITTAL</b> <b>For FY 2007</b>		<b>Complete if Known</b>	
		Application Number	10/692,724-Conf. #9697
		Filing Date	October 27, 2003
		First Named Inventor	Joseph LOSCALZO
		Examiner Name	K. C. Srivastava
<input checked="" type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27		Art Unit	1657
TOTAL AMOUNT OF PAYMENT		(\$)	180.00
		Attorney Docket No.	0102258.00170US3

<b>METHOD OF PAYMENT</b> (check all that apply)	
<input type="checkbox"/> Check	<input type="checkbox"/> Credit Card
<input type="checkbox"/> Money Order	<input type="checkbox"/> None
<input type="checkbox"/> Other (please identify): _____	
<input checked="" type="checkbox"/> Deposit Account	Deposit Account Number: 08-0219
Deposit Account Name: Wilmer Cutler Pickering Hale and	
For the above-identified deposit account, the Director is hereby authorized to: (check all that apply)	
<input checked="" type="checkbox"/> Charge fee(s) indicated below	<input type="checkbox"/> Charge fee(s) indicated below, except for the filing fee
<input checked="" type="checkbox"/> Charge any additional fee(s) or underpayments of fee(s) under 37 CFR 1.16 and 1.17	<input checked="" type="checkbox"/> Credit any overpayments

<b>FEE CALCULATION</b>							
<b>1. BASIC FILING, SEARCH, AND EXAMINATION FEES</b>							
<b>Application Type</b>	<b>FILING FEES</b>		<b>SEARCH FEES</b>		<b>EXAMINATION FEES</b>		<b>Fees Paid (\$)</b>
	<b>Fee (\$)</b>	<b>Small Entity Fee (\$)</b>	<b>Fee (\$)</b>	<b>Small Entity Fee (\$)</b>	<b>Fee (\$)</b>	<b>Small Entity Fee (\$)</b>	
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	
<b>2. EXCESS CLAIM FEES</b>							
<b>Fee Description</b>						<b>Fee (\$)</b>	<b>Small Entity Fee (\$)</b>
Each claim over 20 (including Reissues)						50	25
Each independent claim over 3 (including Reissues)						200	100
Multiple dependent claims						360	180
<b>Total Claims</b>		<b>Extra Claims</b>	<b>Fee (\$)</b>	<b>Fee Paid (\$)</b>	<b>Multiple Dependent Claims</b>		
_____		_____	x _____	= _____	<b>Fee (\$)</b> <b>Fee Paid (\$)</b>		
HP = highest number of total claims paid for, if greater than 20.							
<b>Indep. Claims</b>		<b>Extra Claims</b>	<b>Fee (\$)</b>	<b>Fee Paid (\$)</b>			
_____		_____	x _____	= _____			
HP = highest number of independent claims paid for, if greater than 3.							
<b>3. APPLICATION SIZE FEE</b>							
If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).							
<b>Total Sheets</b>		<b>Extra Sheets</b>	<b>Number of each additional 50 or fraction thereof</b>		<b>Fee (\$)</b>	<b>Fee Paid (\$)</b>	
_____		_____	/50 = _____ (round up to a whole number) x _____		= _____		
<b>4. OTHER FEE(S)</b>							
Non-English Specification, \$130 fee (no small entity discount)						<b>Fees Paid (\$)</b>	
Other (e.g., late filing surcharge): 1806 Submission of an Information Disclosure Statement						180.00	

<b>SUBMITTED BY</b>			
Signature	<i>Belinda Lew</i>	Registration No. (Attorney/Agent)	53,212
Name (Print/Type)	Belinda Lew	Telephone	(202) 663-6000
		Date	September 14, 2007

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Dated: September 14, 2007	Signature: <i>Belinda Lew</i> (Belinda Lew)



Docket No.: 0102258.00170US3  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant:	Joseph LOSCALZO et al.	Confirmation No.:	9697
Application No.:	10/692,724	Art Unit:	1657
Filed:	October 27, 2003	Examiner:	K. C. Srivastava
Title:	METHODS OF TREATING VASCULAR DISEASES CHARACTERIZED BY NITRIC OXIDE INSUFFICIENCY		

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**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT (IDS)**

Dear Sir:

This Information Disclosure Statement is being filed after the mailing date of the first Office Action on the merits and before the mailing date of a final Office Action or a Notice of Allowance.

Please charge the \$180.00 fee to our Deposit Account No. 08-0219.

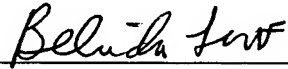
Per the Examiner's request, Applicants are providing copies of the foreign patent and non-patent literature documents cited in the IDS originally filed with the application on October 27, 2003 and re-filed on October 17, 2006.

09/17/2007 DEMMANU1 00000007 080219 10692724  
01 FC:1806 180.00 DA

Applicants request that the Examiner initial and return a copy of the enclosed Form PTO SB-08 with the next communication.

Respectfully submitted,

Dated: September 14, 2007

A handwritten signature in cursive script, appearing to read "Belinda Lew", is written over a horizontal line.

Belinda Lew  
Registration No.: 53,212  
Attorney for Applicant(s)

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Washington, DC 20006  
(202) 663-6000 (telephone)  
(202) 663-6363 (facsimile)



Used in Lieu of PTO/SB/08A/B  
(Based on PTO 04-07 version)

Substitute for form 1449/PTO			<b>Complete if Known</b>		
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Use as many sheets as necessary)</i>			Application Number	10/692,724-Conf. #9697	
			Filing Date	October 27, 2003	
			First Named Inventor	Joseph LOSCALZO	
			Art Unit	1657	
			Examiner Name	K. C. Srivastava	
Sheet	1	of	3	Attorney Docket Number	0102258.00170US3

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)				
	BA	WO-95/26725	10-12-1995	Isis Pharma Gmbh et al.		
/	BB	WO-98/21193	05-22-1998	Del Soldato		✓
	BC	WO-99/00361	01-07-1999	Del Soldato		✓
	BD	WO-99/66921	12-29-1999	Univ Leland Stanford Junior		
	BE	WO-99/67231	12-29-1999	Nicox Sa et al.		✓

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	CA	Bauer, J and Fung, H., "Concurrent Hydralazine Administration Prevents Nitroglycerin-Induced Hemodynamic Tolerance in Experimental Heart Failure," 84(1): 35-39 (1991)	
	CB	Biddle, T., et al., "Comparison of the Effects of Dopamine, Hydralazine, and Isosorbide Dinitrate on Myocardial Hemodynamics in Patients with Refractory Heart Failure," J. Clin. Pharmacol., 21:343-350 (1981)	
	CC	Biegelson, E. and Loscalzo, J., "Endothelial Function and Atherosclerosis," Coronary Artery Disease, Vol. 10, No. 4, pp. 241-256 (1999)	
	CD	Burnier, M., et al., "Salt-Dependent Renal Effects of an Angiotensin II Antagonist in Healthy Subjects," Hypertension, 22(3):339-347 (September 1993)	
	CE	Carson, P., et al., "Race and Hypertensive History Moderate Plasma Renin Activity and Therapeutic Response in Heart Failure: Vasodilator in Heart Failure Trial (HeFT II)," Circulation, Supplement 1, 92(8):I31-I32, Abstract No. 0145 (1995)	
	CF	Carson, P., et al., "Racial Differences in Response to Therapy for Heart Failure: Analysis of the Vasodilator-Heart Failure Trials," Journal of Cardiac Failure, Vol. 5, No. 3, pp. 178-187, September 10, 1999	
	CG	Cohn, J., et al., "A Comparison of Enalapril With Hydralazine-Isosorbide Dinitrate in the Treatment of Chronic Congestive Heart Failure," The New England Journal of Medicine, 325(5):303-310 (1991)	
	CH	Cohn, J., et al., "Effect of Vasodilator Therapy on Mortality in Chronic Congestive Heart Failure," The New England Journal of Medicine, 314(24):1547-1552 (1986)	
	CI	Dries, D., et al., "Racial Differences in the Outcome of Left Ventricular Dysfunction," The New England Journal of Medicine, Vol. 340, No. 8, pp. 609-616, February 25, 1999	
	CJ	Dupuis, J., "Nitrates in Congestive Heart Failure," Cardiovascular Drugs and Therapy,	

Examiner Signature	Date Considered
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Substitute for form 1449/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Use as many sheets as necessary)</i>			<b>Complete if Known</b>		
			Application Number	10/692,724-Conf. #9697	
			Filing Date	October 27, 2003	
			First Named Inventor	Joseph LOSCALZO	
			Art Unit	1657	
			Examiner Name	K. C. Srivastava	
Sheet	2	of	3	Attorney Docket Number	0102258.00170US3

		8(3):501-507 (1994)	
	CK	Franciosa, Joseph, et al., "Immediate Effects of Hydralazine-Isosorbide Dinitrate Combination on Exercise Capacity and Exercise Hemodynamics in Patients with Left Ventricular Failure," <i>Circulation</i> , Vol. 59, No. 6, pp. 1085-1091 (1979)	
	CL	Francis, G., et al., "Plasma Norepinephrine, Plasma Renin Activity, and Congestive Heart Failure, Relations to Survival and the Effects of Therapy in V-HeFTII," <i>Circulation</i> , Supplement VI, 87(6): V140-V148 (1993)	
	CM	Freedman, J. and Loscalzo, J., "Endothelial Dysfunction and Atherothrombotic Occlusive Disease," <i>Drugs</i> , 54 (Supp. 3): 41-50 (1997)	
	CN	Hammerman, S., et al., "Endothelial Cell Nitric Oxide Production in Acute Chest Syndrome," <i>Am. J. Physiol.</i> , 277(46):H1579-H1592 (1999)	
	CO	Hibiya, K., et al., "Hemodynamic and Clinical Effects of Combined Oral Hydralazine and Isosorbide Dinitrate Therapy in Patients With Chronic Refractory Heart Failure," <i>Japanese Circulation Journal</i> , 45:966 (Abstract No. 338) (1981)	
	CP	Johnson, R., "Study Reports Lower Mortality With Hydralazine-Isosorbide Dinitrate Therapy in Mild to Moderate Heart Failure," <i>Clinical Pharmacy</i> , Vol. 5, pages 536 and 541 (1986)	
	CQ	Kaplan, N., et al., "The Intravenous Furosemide Test: A Simple Way to Evaluate Renin Responsiveness," <i>Annals of Internal Medicine</i> , 84:639-645 (1976)	
	CR	Lanas, F., et al., "Tratamiento De La Insuficiencia Cardiaca Avanzada Con Hidralazina E Isorbide," <i>Rev. Med. Chile</i> , 107:926-930 (1979)	
	CS	Leier, C., et al., "Hydralazine and Isosorbide Dinitrate: Comparative Central and Regional Hemodynamic Effects When Administered Alone or in Combination," <i>Circulation</i> , 63(1):102-109 (1981)	
	CT	Loscalzo, et al., "Nitric Oxide Insufficiency and Arterial Thrombosis," <i>Transactions of the American and Climatological Ass.</i> , 11:158-163 (2000)	
	CU	Magorien, R., et al., "Comparative Central and Regional Hemodynamic Effects of Isosorbide Dinitrate and Hydralazine, Alone or in Combination, in Congestive Heart Failure," <i>Clinical Research</i> , 27(4):617A (1979)	
	CV	Massie, B., et al., "Hemodynamic Advantage of Combined Administration of Hydralazine Orally and Nitrates Nonparenterally in the Vasodilator Therapy of Chronic Heart Failure," <i>The American Journal of Cardiology</i> , 40:794-801 (1977)	
	CW	Massie, B., et al., "Postural Hypotension and Tachycardia During Hydralazine-Isosorbide Dinitrate Therapy for Chronic Heart Failure," <i>Circulation</i> , 63(3):658-664 (1981)	
	CX	Massie, B., et al., "Vasodilator Treatment with Isosorbide Dinitrate and Hydralazine in Chronic Heart Failure," <i>Br. Heart J.</i> , 45:376-384 (1981)	
	CY	Nelson, G., et al., "Arteriolar or Venous Dilatation in Left Ventricular Failure, Following Acute Myocardial Infarction: A Haemodynamic Trial of Hydralazine and Isosorbide Dinitrate," <i>Journal of Cardiovascular Pharmacology</i> , 5(4):574-579 (1983)	
	CZ	Pierpont, G., et al., "Combined Oral Hydralazine-Nitrate Therapy in Left Ventricular Failure," <i>Chest</i> , 73(1):8-13 (1978)	
	CA1	Rector, T., et al., "Evaluation by Patients With Heart Failure of the Effects of Enalapril Compared with Hydralazine Plus Isosorbide Dinitrate on Quality of Life - V-HeFT II," <i>Circulation</i> , 87(6): VI-71 - VI-77 (1993)	
	CB1	Rudd, M., et al., "Salt-induced Hypertension in Dahl Salt-resistant and Salt-sensitive Rats with NOS II Inhibition," <i>Am. J. Physiol.</i> , 277 (46):H732-H739 (1999)	
	CC1	Sherman, D., et al., "Endothelial Dysfunction and Cardiovascular Disease," <i>Cardiologia</i> , 42(2):177-187 (1997)	
	CD1	The SOLVD Investigators, "Effect of Enalapril on Mortality and the Development of Heart Failure in Asymptomatic Patients with Reduced Left Ventricular Ejection Fractions," <i>The New</i>	

Examiner Signature		Date Considered	
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Substitute for form 1449/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Use as many sheets as necessary)</i>				<b>Complete if Known</b>	
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				Art Unit	1657
				Examiner Name	K. C. Srivastava
Sheet	3	of	3	Attorney Docket Number	0102258.00170US3

		England Journal of Medicine, 327(10):685-691 (1992)	
	CE1	Turner, G., et al., "Reassessment of Vasodilator Therapy in Angina: Effectsof Oral Isosorbide Ddiitrate and Hydralazine on Exercise Tolerance in Patients Receiving Propranolol," The American Journal of Cardiology, 57:910-916 (1981)	
	CF1	Turner, G., et al., "Vasodilator Therapy in Angina: Effects of Isosorbide Dinitrate and Hydralazine on Exercise Tolerance During Propranolol Therapy," Clinical Research, 29(2):246A (1981)	
	CG1	Üsdin, J., et al., "La Place Des Vasodilateurs Oraux dans le traitement de l'insuffisance Cardiaque," Coeur, 10(1):119-128 (1979)	√
	CH1	von Lutterotti, N., et al., "Angiotensin II Receptor Antagonist Markedly Reduces Mortality in Salt-Loaded Dahl S Rats," American Journal of Hypertension, 4(4 Part 2):346S-349S (1991)	
	CI1	Wilson, J., et al., "Circulatory Improvement After Hydralazine or Isosorbide Dinitrate Administration in Patients with Heart Failure," The American Journal of Medicine, Vol. 71, pp. 627-633 (1981)	
	CJ1	Ziesche, S., et al., "Hydralazine and Isosorbide Dinitrate Combination Improves Exercise Tolerance in Heart Failure - Results from V-HeFT I and V-HeFT II," Circulation, 87(6): VI-56-VI-64 (1993)	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>Applicant is to place a check mark here if English language Translation is attached.

Examiner Signature		Date Considered	
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